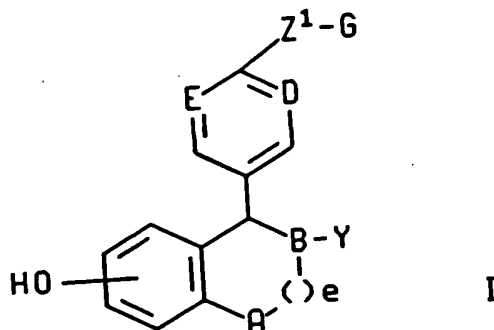


CLAIMS

1. A method of inhibiting a pathological condition which is susceptible or partially susceptible to inhibition by an estrogen, antiestrogen or estrogen agonist, which comprises administering to a mammal in need of inhibition of said pathological condition selected from the group consisting of uterine cancer, adjuvant breast cancer, breast disorders, male breast cancer, migraine, incontinence, vaginal atrophy, bladder infection, senile gynecomastia, diabetes, hyperglycemia, failure of wound healing, melanoma, impotence, inflammatory bowel disease, CNS and GI disorders caused by an excess of tachykinins, decreased libido, immune system disorders, decreased fertility, pulmonary hypertensive disease, acne, seborrhea, autoimmune disease, Turner's syndrome, alopecia, hirsutism, disorders related to an excess of neurokinin and obsessive-compulsive disorders including smoking and alcohol abuse, an effective amount of a compound of formula I



wherein:

A is selected from CH₂ and NR;

B, D and E are independently selected from CH and N;

Y is

- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (c) C₃-C₈ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R⁴;
- (d) C₃-C₈ cycloalkenyl, optionally substituted with 1-2 substituents independently selected from R⁴;

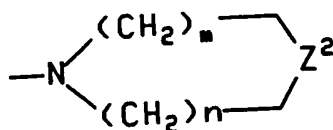
- 5
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n-, optionally substituted with 1-3 substituents independently selected from R⁴;
- (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n-, optionally substituted with 1-3 substituents independently selected from R⁴; or
- 10 (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -NR²-, and -S(O)_n-, optionally substituted with 1-3 substituents independently selected from R⁴;

Z¹ is

- 15
- (a) -(CH₂)_p W(CH₂)_q-;
- (b) -O(CH₂)_p CR⁵R⁶-;
- (c) -O(CH₂)_p W(CH₂)_q-;
- (d) -OCHR²CHR³-; or
- (e) -SCHR²CHR³-;

20 G is

- (a) -NR⁷R⁸;
- (b)



25

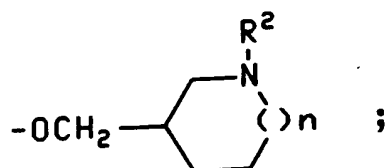
wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R⁴;

30 or

- (c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R^4 ;

Z^1 and G in combination may be

5



W is

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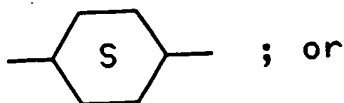
- (a) $-CH_2-$;
- (b) $-CH=CH-$;
- (c) $-O-$;
- (d) $-NR^2-$;
- (e) $-S(O)_n-$;
- (f)

15



20

- (g) $-CR^2(OH)-$;
- (h) $-CONR^2-$;
- (i) $-NR^2CO-$;
- (j)



25

- (k) $-C \equiv C-$;

R is hydrogen or C_1-C_6 alkyl;

R^2 and R^3 are independently

30

- (a) hydrogen; or
- (b) C_1-C_4 alkyl;

R^4 is

- (a) hydrogen;
- (b) halogen;

- 5 (c) C₁-C₆ alkyl;
 (d) C₁-C₄ alkoxy;
 (e) C₁-C₄ acyloxy;
 (f) C₁-C₄ alkylthio;
 (g) C₁-C₄ alkylsulfinyl;
 (h) C₁-C₄ alkylsulfonyl;
 (i) hydroxy (C₁-C₄)alkyl;
 (j) aryl (C₁-C₄)alkyl;
 (k) -CO₂H;
 10 (l) -CN;
 (m) -CONHOR;
 (n) -SO₂NHR;
 (o) -NH₂;
 (p) C₁-C₄ alkylamino;
 15 (q) C₁-C₄ dialkylamino;
 (r) -NHSO₂R;
 (s) -NO₂;
 (t) -aryl; or
 (u) -OH.
- 20 R⁵ and R⁶ are independently C₁-C₆ alkyl or together form a C₃-C₁₀ carbocyclic ring;
 R⁷ and R⁸ are independently
- 25 (a) phenyl;
 (b) a C₃-C₁₀ carbocyclic ring, saturated or unsaturated;
 (c) a C₃-C₁₀ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
 (d) H;
 (e) C₁-C₆ alkyl; or
 (f) form a 3 to 8 membered nitrogen containing ring with R⁵ or R⁶;
- 30 R⁷ and R⁸ in either linear or ring form may optionally be substituted with up to three substituents independently selected from C₁-C₆ alkyl, halogen, alkoxy, hydroxy and carboxy;
 a ring formed by R⁷ and R⁸ may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

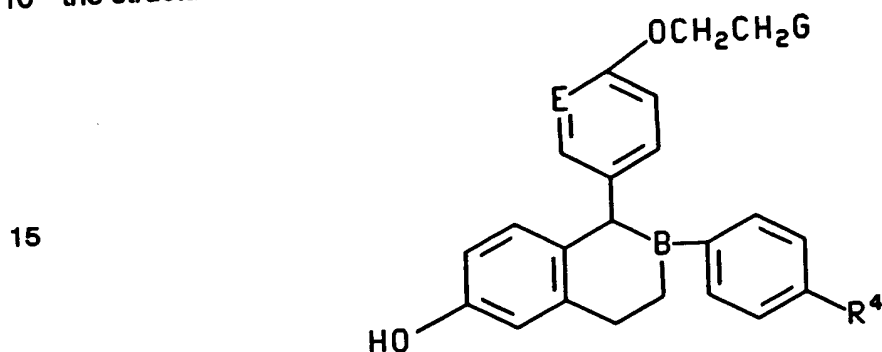
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

5 q is 0, 1, 2 or 3;

and optical and geometric isomers thereof; and nontoxic pharmacologically acceptable acid addition salts, N-oxides, esters, and quaternary ammonium salts thereof.

2. A method of Claim 1 wherein the compound of formula 1 is a compound of
10 the structure



wherein G is

20



3. A method of Claim 1 wherein the compound of formula 1 is selected from
25 the group consisting of

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol,

(-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol,

30 Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol,

Cis 1-[6'-pyrrolodinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydro-naphthalene,

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4'-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline,

Cis-6-(4'-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalen-2-ol, and

- 5 1-(4'-Pyrrolidinoethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline.
4. A method of claim 1 wherein said pathological condition is a breast disorder.
5. A method of claim 1 wherein said pathological condition is vaginal atrophy.
6. A method of claim 1 wherein said pathological condition is a bladder
- infection.
- 10 7. A method of claim 1 wherein said pathological condition is senil gynecomastia.
8. A method of claim 1 wherein said pathological condition is diabetes.
9. A method of claim 1 wherein said pathological condition is hyperglycemia.
10. A method of claim 1 wherein said pathological condition is failure of wound
- 15 healing.
11. A method of claim 1 wherein said pathological condition is decreased libido.
12. A method of claim 1 wherein said pathological condition is an immun
- system disorder.
13. A method of claim 1 wherein said pathological condition is decreased
- 20 fertility.
14. A method of claim 1 wherein said pathological condition is pulmonary hypertensive disease.
15. A method of claim 1 wherein said pathological condition is acne.
16. A method of claim 1 wherein said pathological condition is seborrhea.
- 25 17. A method of claim 1 wherein said pathological condition is autoimmun
- disease.
18. A method of claim 1 wherein said pathological condition is Turn r's Syndrome.
19. A method of claim 1 wherein said pathological condition is hirsutism.
- 30 20. A method of claim 1 wherein said pathological condition is alopecia.
21. A method of claim 1 wherein said pathological condition is an obsessive-compulsive disorder.

22. A method of claim 1 wherein said pathological condition is undesired pregnancy.